Remarks/Arguments

Claims 1-26 were examined in this case. Claims 1-26 stand rejected. Each of the objections and rejections raised in the Office Action is addressed individually below.

Claims 1, 3, 5, 8, 10, 11, 12, 13, 15, 17, 20, 23, and 24 have been amended primarily to clarify the claim language and to achieve consistency in the language used throughout the claims. No new matter is introduced as a result of these amendments. Thus, Applicant respectfully requests their entrance by the Examiner.

Rejection Under 35 U.S.C. § 102(e)

Claims 1-26 stand rejected as being unpatentable under 35 U.S.C. §102(e) as being anticipated by Vivekananda et al. (U.S. Patent No. 6,569,630) and Kutyavin et al. (U.S. Patent No. 5,912,340). The Examiner maintains the reasons for rejection levied in the Office Action mailed October 2, 2003 in which she asserts that the two references teach methods comprising synthesizing nucleic acid molecules with reduced levels of cross hybridization through the utilization of nucleotides recited in the currently pending claims. Applicant respectfully submits that neither reference anticipates the currently pending claims.

Contrary to the Examiner's assertion, Vivekananda *et al.* do not teach methods of synthesizing nucleic acid molecules with reduced levels of cross hybridization. Vivekananda *et al.* disclose a method of detecting anthrax spores and other chemical and biological agents. They achieve this by utilizing nucleic acid molecules that are able to specifically bind particular targets, preferably through non-Watson-Crick interactions. Specifically, Vivekananda *et al.* define their preferred nucleic acid aptamers as "a nucleic acid that binds to another molecule ('target' as defined below). *This binding interaction does not encompass standard nucleic acid/nucleic acid hydrogen bond formation exemplified by Watson-Crick basepair formation (e.g., A binds to U or T and G binds to C), but encompasses all other types of non-covalent (or in some cases covalent) binding.*" (column 8, lines 27-33, emphasis added). The intended binding target of Vivekanada et al.'s nucleic acids are "any compound or aggregate of interest. Non-limiting examples include a protein, peptide, carbohydrate, polysaccharide, glycoprotein, lipid, hormone, receptor, antigen, allergen, antibody, substrate, metabolite, cofactor, inhibitor, drug,

pharmaceutical, nutrient, toxin, cholera toxin, Shiga-like toxin, poison, explosive, pesticide, chemical warfare agent, biohazardous agent, prion, radioisotope, vitamin, heterocyclic aromatic compound, carcinogen, mutagen, narcotic, amphetamine, barbiturate, hallucinogen, waste product, contaminant or other molecule" (column 8, lines 46-56). Thus, Vivekananda et al. do not teach a method of synthesizing nucleic acids with reduced levels of cross hybridization, but instead teach a method of synthesizing nucleic acids that bind to their intended non-nucleic acid targets with greater affinity via non-Watson-Crick-type interactions.

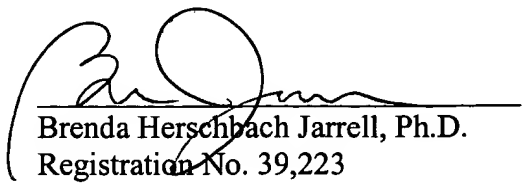
By contrast, the invention recited in the presently pending claims is directed to methods of synthesizing nucleic acid molecules that include nucleotides that "have a reduced ability to form stable hydrogen bonded base pairs with each other, but can form stable hydrogen bonded base pairs with [their] complementary naturally occurring nucleotide[s]..." (see claims 1 and 12). Thus, the invention recited in the presently pending claims teaches the synthesis of nucleic acid molecules that do bind to certain nucleic acid molecules via traditional Watson-Crick-like hydrogen bonding interactions. Vivekananda *et al.* simply do not teach or suggest such a method. In fact, by stating that their invention "does not encompass standard nucleic acid/nucleic acid hydrogen bond formation" (col. 8, lines 28-30), Vivekananda *et al.* actually teach away from the invention recited in the currently pending claims, and thus cannot anticipate the present claims.

Kutyavin *et al.* disclose a matched set of oligonucleotides containing modified nucleotides such that each member of the matched set is able to hybridize with a complementary strand in a duplex nucleic acid molecule, but is unable to hybridize with the other member of the matched set. The invention of Kutyavin *et al.* addresses the specific problem of facilitating strand invasion of a duplex nucleic acid molecule (see col. 1, lines 15-36) since the matched set of complementary oligonucleotides will not bind each other. Thus, each member of the matched set will be available to invade a duplex nucleic acid molecule. The key inventive feature disclosed by Kutyavin *et al.* is that the matched set of oligonucleotides must be unable to base pair with <u>each other</u> (see col. 1, lines 51-53, "Thus, the matched pair of oligonucleotides in accordance with the present invention do not form substantially stable hydrogen bonded hybrids with *one another*..." (emphasis added)). However, Kutyavin *et al.* do not teach or suggest a method of producing nucleic acid molecules that contain pairs of nucleotides such that the nucleic acid molecules: 1) are unable to base pair with each other, and 2) are individually unable

to form intramolecular base pair interactions. In contrast, the currently pending claims recite a method of producing nucleic acid molecules that not only have a reduced ability to form stable hydrogen bonded base pairs with each other, but also have a reduced ability to form stable hydrogen bonded intramolecular base pair interactions. The reduced ability of the molecules produced in accordance with the present claims to form both intermolecular and intramolecular hydrogen bonded base pairs stems from the fact that both members of a non-hydrogen bond forming nucleotide pair are necessarily present in each nucleic acid molecule produced. For example, independent claim 1 recites a method of synthesizing nucleic acid molecules by providing a collection of nucleotides that includes "at least one pair of complementary nucleotides that have a reduced ability to form a stable hydrogen bonded base pair with each other, wherein each member of said pair can form a stable hydrogen bonded base pair with its complementary naturally occurring nucleotide" (emphasis added). Similarly, independent claim 12 recites a method of producing nucleic acid molecules by providing a collection of nucleotides that includes "pairs of complementary nucleotides that have a reduced ability to form a stable hydrogen bonded base pair with each other, wherein each member of said pair can form a stable hydrogen bonded base pair with its complementary naturally occurring nucleotide" (emphasis added). The matched set of oligonucleotides disclosed in Kutyavin *et al.* contains no such limitation and thus cannot anticipate the currently pending claims.

In light of the following Amendments and Remarks, Applicant respectfully submits that the present case is in condition for allowance. A Notice to that effect is respectfully requested.

Respectfully Submitted,



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